REMARKS

By the foregoing Amendment, Claims 1 and 3-5 are amended and Claim 2 is cancelled. Entry of the Amendment, and favorable consideration thereof is earnestly requested. Claims 6-37 have previously been withdrawn from consideration. Claims 1 and 3-5 remain pending.

The Examiner has noted that the application does not contain an Abstract. An abstract is attached hereto on a separate sheet. The Examiner also noted the lack of a cross-reference to related applications, which cross-reference has been added to the Specification.

The Examiner has objected to the Specification as containing abbreviations and as containing improperly used trademarks. Applicant respectfully submits that the abbreviations used in the specification are either defined therein or are so notoriously well-known in the art that definition thereof is not necessary. Therefore, Applicant respectfully asks the Examiner to reconsider this objection or to identify abbreviations which are not so notoriously well-known that they require definition. Applicant has failed to identify any instances of improper trademark usage in the Specification, and therefore respectfully asks the Examiner to identify such improper uses.

Claims 1-5 stand rejected under 35 U.S.C. 112, first paragraph, as being not sufficiently enabled by the specification. Claims 1 and 3-5 have been amended and Claim 2 has been cancelled. To the extent that the Examiner's rejections under 35 U.S.C. 112, first paragraph are still applicable to the claims, as amended, Applicant respectfully requests that the Examiner reconsider these rejections in view of the following remarks.

Applicant respectfully submits that although the examples presented in the Specification are directed to nasal immunization of mice against HSV-1, the Specification provides more than adequate disclosure that the invention is not so limited. Merely because one or more examples are presented does not mean that the invention is limited to those examples. Moreover, in this case, the Specification repeatedly and clearly demonstrates that applications broader than those presented in the examples were contemplated. For example, simply because no actual studies on humans are reported in the Specification does not mean that the application does not enable use in connection with humans. The Examiner is attempting to improperly limit the application to the examples given, even though such examples are not required and are not limiting in any way. If for example, no examples were given at all, according to the Examiner's reasoning, the Specification would not be enabling for any use. Applicant respectfully submits

that this is improper, and respectfully requests that the Examiner reconsider this rejection.

Moreover, Applicant respectfully submits that the Examiner's contention that the data on HSV do not anticipate that EtxB would be of use in developing vaccines against other agents is erroneous. Applicant includes herewith several documents which demonstrate that EtxB is effective with antigens other than HSV-1. The data clearly demonstrate the ability of EtxB to turn a non-immunogenic protein into a highly immunogenic vaccine. This proves beyond doubt its ability to act as an adjuvant. The point of an adjuvant or immune modulator in a vaccine is to potentiate a response to the antigen. The data provided shows that whereas the HSV antigens are not themselves immunogenic when given alone, a potent antibody response (both local and systemic) and an associated T cell response are triggered when the antigens are mixed with EtxB. This alone proves the credentials of EtxB as an adjuvant and the disease protection data simply shows that the presence of such an immune response can have clinical relevance.

Furthermore, the ability of EtxB to promote an antibody and a T cell response is not restricted to its combination with these particular HSV proteins. In separate experiments it has been demonstrated that EtxB is a potent adjuvant for other antigens. These include hen egg lysozyme, ovalbumin and a preparation of

bacterial antigens from *Streptococcus equis*. The findings from these studies demonstrate the broad applicability of EtxB as an adjuvant/modulator capable of promoting a robust immune response to an admixed antigen. As disclosed in the present application, Applicant has improved upon the prior art, however, by discovering how to make EtxB effective at stimulating the immune response to a vaccine, and this is what is claimed.

It will be clear to those skilled in the art that the method discovered by Applicant is useful for a variety of subjects in conjunction with vaccines for a variety of diseases. When the disclosure of the Specification is taken in conjunction with what is known in the prior art (as demonstrated by the attached documents), one skilled in the art must only perform routine experimentation to use the invention to the fullest extent claimed. As such, Applicant respectfully submits that Claims 1 and 3-5, as amended, are enabled by the Specification.

Claims 1-5 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Claims 1 and 3-5 have been amended to obviate some of the offensive terminology. With respect to the term "free from whole toxin", Applicant respectfully submits that this term is intended to have its plain and ordinary meaning. More specifically, the EtxB subunit does not

form a part of the whole toxin (i.e., only a subunit of the whole toxin -- the EtxB subunit -- is present). This is explained in the specification as filed, inter alia, at page 1, line 8 through page 2, line 13.

The Examiner has rejected all pending claims either under 35 U.S.C. §102(b) as being anticipated by Holmgren et al. (U.S. Patent No. 5,681,571) or under 35 U.S.C. §103(a) as being unpatentable over Clements (U.S. Patent No. 6,413,523 B1) in view of Marcello et al. (Proc. Natl. Acad. Sci. USA, Vol. 91, pp. 8894-8998, September 1994). Applicant respectfully asks the Examiner to reconsider these rejections in view of the above Amendments and the below Remarks.

All pending claims as amended require a method for stimulating an immune response to a vaccine applied to a mammalian subject comprising the step of administering to the subject an effective amount of EtxB or a molecule having substantially equivalent activity, free from whole toxin and not linked to an antigen. Applicant respectfully submits that none of the cited prior art, either alone or in combination, discloses, teaches or suggests such a method.

With respect to Clements, this reference teaches using only the whole toxin E. coli heat labile enterotoxin (LT). It should be noted that this is precisely the

prior art which Applicant distinguished in the background section of its application at page 1, lines 8-26. Clements does not disclose, teach or suggest in any way stimulating an immune response by the subunit EtxB which is free of (i.e., does not form a part of) whole toxin.

Similarly, Marcello et al. is distinguished because it is taught therein that the EtxB is linked to a specific peptide and not administered freely with a vaccine, as required by all claims as amended. Marcello et al. does not disclose, teach or suggest in any way that EtxB free of whole toxin when administered to a mammal stimulates an immune response to a vaccine. Moreover, the Marcello et al. peptide is itself capable of inhibiting the activity of an enzyme which is critical to HSV replication. Therefore, the teachings of this reference have nothing to do with vaccination or the induction of a protective immune response and cannot be applied to any other peptide.

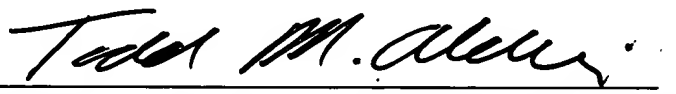
Holmgren et al. is distinguished from the present invention as claimed for several reasons. First, it is taught in Holmgren et al. that EtxB is linked to the antigen and not freely given with a vaccine. Secondly, the teachings of Holmgren et al. relate to inducing immunological tolerance which equates to reducing an immune response rather than to stimulating an immune response to a vaccine in

order to assist the activity of a vaccine against a particular condition or disease. This is exactly the opposite of what is claimed.

Thus, none of the prior art, either alone or when properly combined, discloses, teaches or suggests a method for stimulating an immune response to a vaccine applied to a mammalian subject comprising the step of administering to the subject an effective amount of EtxB or a molecule having substantially equivalent activity, free from whole toxin and not linked to an antigen.

For the foregoing reasons, Applicant respectfully submits that all pending claims, namely Claims 1 and 3-5, are patentable over the references of record, and earnestly solicits allowance of the same.

Respectfully submitted,



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